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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,290	05/09/2005	Toshiyuki Takasu	Q87757	9818
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/534,290	Applicant(s) TAKASU ET AL.
	Examiner CHARLESWORTH RAE	Art Unit 1611

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 03 April 2008.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-10 is/are pending in the application.
 - 4a) Of the above claim(s) is/are withdrawn from consideration.
- 5) Claim(s) is/are allowed.
- 6) Claim(s) 1-10 is/are rejected.
- 7) Claim(s) is/are objected to.
- 8) Claim(s) are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. .
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date:
- 5) Notice of Informal Patent Application
- 6) Other:

DETAILED ACTION

Acknowledgement is made of applicants' filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.1114.

Status of the Claims

Claims 1-10 are currently pending in this application and are the subject of the Office action.

Claim 4 has been amended.

Claim Amendments

Applicant's claim amendment, received 2/11/08, is acknowledged. It is noted that claim 4 has been amended to recite the term "urge."

Priority Claim

Applicant's statement that a certified copy of the English translation of priority application JP Application No. 2002-323792 (see applicant's Response, page 4, last para to page 5, line 4), is acknowledged. However, it is noted that the examiner has not been able to locate said document.

Information Disclosure Statement

Consideration of applicant's previously filed information disclosure statements have been duly considered; an initialed copy is attached herewith (see applicant's Response, page 4, as well).

Response to applicant's arguments/remarks

Nonstatutory obviousness-type double patenting (ODP) rejection

Applicant contends that these rejections should be withdrawn for essentially the following summarized reasons (see applicant's Response, pages 5-10):

- 1) The treatment of diabetic patients with the claimed compound does not necessarily perform the claimed method, as is required to establish inherency, because the diabetic patients do not necessarily suffer from overactive bladder.
- 2) The cited references teach away from using the claimed compound for treatment of diabetes because administration of the claimed compound, an anticholinergic agent, would result in further decrease in bladder detrusor activity, resulting in greater incontinence, if used to treat bladder atony in diabetics; it would be counterintuitive to the treatment of urinary overflow incontinence in patients with diabetes.

In response, the rejection is maintained as applicant's arguments are not found to be persuasive to overcome the rejection of record for the reasons previously made of record in the Office action mailed 11/15/07 at pages 6-8.

Rejection under 102(b)

Applicant contends that these rejections should be withdrawn for essentially the following summarized reasons (see applicant's Response, pages 10 -11):

- 1) Maryuma is directed to amide derivatives represented by general formula (I), and is disclosed to be useful as a diabetes remedy. However, Maryuma does not explicitly or inherently disclose the instant claimed method for treating overactive bladder.
- 2) Maryuma teaches away from using the claimed compound for treatment of diabetes because administration of the claimed compound (which is an anticholingeric), would result in a further decrease in bladder detrusor activity and greater incontinence.

3) Administration of the claimed compound would be counterintuitive to the treatment of urinary overflow incontinence in patients with diabetes.

In response, the rejection is maintained as applicant's arguments are not found to be persuasive to overcome the rejection of record for the reasons made of record in the Office action, mailed 11/115/07, at pages 8-9. In addition, it is the examiner's position that a) applicant's assertion that it would be counterintuitive to practice the instant claimed method in treating urinary overflow incontinence in patients with diabetes is not supported by any objective evidence, b) there is a clear nexus between bladder overactivity, urinary incontinence, and diabetes as evidenced by the teaching of Cecil (already made of record, pages 23-24, and 637-642), and c) the scope of claims 1-3, 6-10 exceeds the scope of "urge incontinence."

Anticipation under 35 USC 102 is an essentially irrebuttable question of fact, wherein the court stated that anticipation "cannot be overcome by evidence of unexpected results or teachings away in the art". *In re Malagari*, 499 F.2d 1289, 182 USPQ; *In re Spada*, 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990); *In re Fracalossi*, 681 F.2d 792, 215 USPQ 569 (CCPA 1982); *In re Alternpohl*, 500 F.2d 1151, 183 USPQ 38 (CCPA 1974); *In re Wiggins*, 488 F.2d 538, 179 USPQ 421 (CCPA 1973); *In re Wilder*, 429 F.2d 447, 166 USPQ 545 (CCPA 1970). Indeed, a reference might reside in a nonanalogous art and yet constitute an anticipation of a claimed invention under 35 USC 102. *In re Self*, 571 F.2d 134, 213 USPQ 1 (CCPA 1982).

REJECTIONS

Nonstatutory Obviousness-Type Double-Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 13 in view of claim 6 of U.S. Patent 6,346,532 (‘532), in view of Cecil Textbook of Medicine. 2000, vol. 1, pages 23-24, and 637-642, especially page 23, col. 1, last para and page 640, col. 1, 3rd para). Although the conflicting claims are not

identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims. In particular, In particular, reference claim 13 is directed to a method of treating diabetes comprising administering a compound having the same general formula which encompasses the compound species recited in instant claim 1; reference claim 6 of reference '532 is drawn in part to the instant claimed compound:

(R)-2-(2-aminothiazol-4-yl)-4'[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide.

The rejection made of record in the Office action mailed Office, mailed 11/15/07, at pages 6-8 is incorporated by reference.

Thus, claims 1-10 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 13 in view of claim 6 of U.S. Patent 6,346,532 ('532) in view of Cecil's.

Claim rejections – 35 USC 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10 are rejected under 35 USC 102(b) as being anticipated by Maruyama et al. (WO99/20607; equivalent English translation U.S. Patent 6,346,532 B1).

Maruyama et al. teach the instant claimed composition comprising compound (R)-2-(2-aminothiazol-4-yl)-4'[2-(2-hydroxy-2phenylethyl)amino]ethyl]acetanilide (see claim 6 and Example 36) recited in instant claims 1 and 6. Maruyama et al. teach methods for treating

diabetes comprising administering an effective amount of the drug for treating said diabetes.

Instant claim 1 recites “[a] method for treating overactive bladder.” To the extent that the diabetic population overlaps with the instant claimed overactive bladder treatment population as evidenced by the teaching of Cecil’s, as discussed above in connection with the Response to applicant’s arguments/remarks, the contemplated treatment effects in practicing the instant claimed invention are deemed to be inherent features of administering (R)-2-(2-aminothiazol-4-yl)-4’-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide. The limitations with respect to “overactive bladder is a result of benign prostatic hyperplasia,” as recited in claims 2 and 7; “wherein the subject has urinary urgency,” as recited in claims 3 and 8; “wherein the subject as urinary incontinence,” as recited in claims 4 and 9; “wherein the subject has pollakiuria,” as recited in claims 5 and 10, are deemed to be inherent characteristics of practicing the instant claimed method.

Cecil (already made of record) is added for evidentiary purposes in support of examiner’s position that a nexus exist between overactive bladder and diabetes/benign prostatic hypertrophy. Cecil teaches that the most common cause of urinary incontinence in elderly men and women is overactive bladder as evidenced by the teaching of Cecil Texbook of Medicine. 2000, vol. 1, pages 23-24, and 637-642, especially page 23, col. 1, last para and page 640, col. 1, 3rd para). Cecil’s teaches that urge incontinence is the most common and bothersome symptomatic type of urinary incontinence in the geriatric population and is usually associated with other symptoms of bladder overactivity such as daytime frequency and nocturia; men, diabetics, and patients with neurologic disorders are at highest risk for this type of urinary incontinence (page 640, col. 2, 4th

para). Cecil also teaches that urinary incontinence is a common manifestation of benign and malignant prostate enlargement in middle-aged and older men (page 640, col. 1, 3rd para).

To the extent that the treatment population overlaps with the diabetic patient population, coupled with the fact that the only active method step is the administering of a known drug for treating diabetes, the contemplated treatment effects in practicing the instant claimed method are deemed to be inherent characteristics of the instant claimed method. Thus, claims 1-10 are found to be anticipated.

Claim rejections – 35 USC 103(a) – Newly applied

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

¹Alternatively, claims 1-10 are rejected under 103(a) as being unpatentable over Maruyama et al. (WO99/20607; equivalent English translation U.S. Patent 6,346,532 B1), in view of Cecil and Fabiano et al. (US patent 6,204,285).

The above discussions of Maruyama et al. and Cecil in connection with the rejection under 102(b) is incorporated by reference.

Fabiano et al. (US patent 6,204,285) is added to show the general state of the art regarding the use of anticholinergic drugs in treating urinary incontinence. Fabiano et al. teach methods of treating urinary incontinence, such as incontinence resulting from bladder detrusor instability, stress incontinence, overflow incontinence, urge incontinence, comprising administering an anticholinergic agent, glycopyrrolate (abstract; col. 1, line 23 to col. 3, line 7; see especially, col. 2, line 60 to col. 3, line 1). Fabiano et al. teach that no treatment for incontinence, including existing drug therapies, has achieved complete success with all classes of incontinent patients, and without significant side effects (col. 1, line 65 to col. 2, line 16).

Based on the teaching of Fabiano et al. that no treatment for incontinence has achieved complete success, and without significant side effects, someone of skill in the art would have been motivated to combine the above cited references to create the instant claimed inventive concept.

Thus, someone of skill in the art at the time the claimed invention was made would have found it obvious to create the instant claimed invention with reasonable predictability.

Relevant Art of Record

The below art made of record and relied upon are considered pertinent to applicant's invention.

Cruz et al. (US Patent 6,630,515) is added to show the general state of the art teach that the clinical term "overactive bladder" is used generally to denote any form of incontinence characterized by increased frequency of micturition or desire to void, whether complete or

episodic, and where loss of voluntary control ranges from partial to total (col. 1, lines 34-39). Cruz et al. teach that "urge incontinence" is the involuntary loss of urine associated with an abrupt and powerful desire to void, which is usually, but not always, associated with the urodynamic finding of involuntary (uninhibited) contractions of the detrusor muscle (col. 1, lines 39-44). Cruz et al. teach that a large subset of patients with uninhibited detrusor have some sort of neurologic impairment, in which case the clinical term is "detrusor hyperreflexia (col. 1, lines 45-57).

Skolnick (US Patent Application Pub. No. 2008/0009538; post art reference) teach the most widely used drug treatment for overactive bladder employs antimuscarinic agents, such as oxybutynin (para 0007). Overactive bladder can involve both peripheral and central control defects, including hypersensitivity of sensory neurons of the bladder (e.g., arising from inflammatory conditions, hormonal imbalances, or prostatic hypertrophy), destruction of the sensory nerve fibers, and damage to the spinal cord or brain stem causing interruption of transmitted signals (para 0006). Neurogenic overactive bladder (or neurogenic bladder) is caused by detrusor hyperreflexia secondary to neurologic disorders such as stroke, Parkinson's disease, diabetes, multiple sclerosis, peripheral neuropathy, or spinal cord injury (para 0006). Non-neurogenic overactive bladder is caused by detrusor muscle instability, arising from non-neurological abnormalities such as bladder stones, muscle disease, urinary tract infection and pharmacological side effects (para 0006). Despite pharmacological advances, there are still no satisfactory treatments for urinary incontinence and associated conditions caused by disorders of the lower urinary tract. Accordingly, there

remains an important, unmet need for alternative compositions and methods to treat urinary incontinence and associated conditions caused by neurogenic and non-neurogenic overactive bladder, interstitial cystitis, prostatitis, prostdynia, benign prostatic hyperplasia, and other lower urinary tract disorders in mammalian subjects.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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19 May 2008
/C. R./
Examiner, Art Unit 1611

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614